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August 11, 2003

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DUE ON FEB 11 2004 OL
Amendment

Application No.	:	**2,328,159** / 5430-45CA
Owner	:	JOMAA, HASSAN
Title	:	**USE OF ORGANOPHOSPHORIC COMPOUNDS FOR THE THERAPEUTIC AND PREVENTATIVE TREATMENT OF INFECTIONS**
Classification	:	A61K-31/66
Examiner	:	**Wesley Sharman**

IN ACCORDANCE WITH SUBSECTION 30(2) OF THE PATENT RULES, YOU ARE HEREBY NOTIFIED OF A REQUISITION BY THE EXAMINER. IN ORDER TO AVOID ABANDONMENT UNDER PARAGRAPH 73(1)(A) OF THE PATENT ACT, A WRITTEN REPLY MUST BE RECEIVED WITHIN 6 MONTHS AFTER THE ABOVE DATE.

This application has been examined as originally filed.

The number of claims in this application is 11.

A search of the prior art has revealed the following:

References Applied:

Publications

Camp et al.	Biorg. Med. Chem. Lett.	1992, 2, 1047.

Canadian Patent Documents

2089650	Mar. 5, 1992	Kleiner
2260898	Jan. 29, 1998	Reiter
1261347	Sep. 26, 1989	Bartels
2142348	Mar. 17, 1994	de Lombaert
2185728	Sep. 21, 1995	Smith et al.
1108131	Sep. 1, 1981	von Esch

Camp discloses the antiviral activity of aminophosphonic acids.

von Esch discloses amides of phosphonoacetic acid and their use in treating herpes virus infections.

Bartels discloses aminoalkylphosphonic acid derivatives and their biological activity.

Kleiner discloses aminomethanephosphonic acid derivatives and their biological activity.

de Lombaert discloses phosphono substituted tetrazole derivatives and their ability to inhibit neutral endopeptidases.

Smith et al. disclose aminoalkylphosphonic acid derivatives and their pronounced biological activity including inhibition of proteolytic enzymes.

Reiter discloses aminoalkylphosphonic acid derivatives and their use against AIDS, sepsis, septic shock, periodontal disease and other diseases and infections.

The examiner has identified the following defects in the application:

Claims 1-7 and 9 do not comply with Paragraph 28.2(1)(b) of the Patent Act. Camp disclosed the claimed subject matter before the claim dates.

Claims 1, 4 and 6-9 do not comply with Paragraph 28.2(1)(b) of the Patent Act. Kleiner disclosed the claimed subject matter before the claim dates.

Claims 1 and 5-11 do not comply with Paragraph 28.2(1)(b) of the Patent Act. Reiter disclosed the claimed subject matter before the claim dates.

Claims 1 and 6-9 do not comply with Paragraph 28.2(1)(b) of the Patent Act. Bartels, de Lombaert and Smith et al. all disclosed the claimed subject matter before the claim dates. The use of the aminoalkylphosphonic acid derivatives for inhibiting neutral endopeptidases (as disclosed by de Lombaert) and proteolytic enzymes (as disclosed by Smith et al.) can be viewed as a treatment of infections in humans and animals caused by parasites, fungi and viruses.

Claims 1, 6, 7 and 9 do not comply with Paragraph 28.2(1)(b) of the Patent Act. von Esch disclosed the claimed subject matter before the claim dates.

Claims 10 and 11 do not comply with Section 28.3 of the Patent Act. The subject matter of these claims would have been obvious on the claim date to a person skilled in the art or science to which they pertain having regard to Camp, Kleiner, Bartels, de Lombaert, Smith et al. or von Esch. Pharmaceutical preparations containing multiple active ingredients are well known in the art and there is no suggestion within the present description that the pharmaceutical preparations containing multiple active ingredients defined in claims 10 and 11 give surprising results. As such, it would be obvious to a person skilled in the art to prepare the pharmaceutical preparations containing multiple active ingredients defined in claims 10 and 11.

Note that the definition given in the description for alkylene on page 10, lines 2-4 includes the statement that "the hydrogen atoms may be replaced by other substituents". Therefore, the

alkylene groups may be substituted and the use of the compounds disclosed by Camp, Reiter, Smith et al. and von Esch fall within the scope of claims against which they are cited.

Claims 1-11 do not comply with Section 84 of the Patent Rules. The description fails to provide a sound line of reasoning for the utility of the compounds defined in claims 1-6 for the production of pharmaceutical preparations for the treatment of infections which are caused by the viruses defined in claim 7 or the unicellular parasites defined in claim 8. The factual support described in examples 1-3 does not lead to the conclusion that the subject matter of these claims would have the predicted utility. (Apotex Inc. v. Wellcome Foundation Ltd., 2002 SCC 77). There is substantive support for the use of the compounds defined in claims 1-6 for the preparation of pharmaceutical preparations for the treatment of Plasmodium falciparum, the causative organism of malaria. There is no sound basis for predicting the utility of the compounds of claims 1-6 for the treatment of any other parasite. Nor is there any substantive support or sound prediction for the utility of the compounds defined in claims 1-6 for the treatment of viruses and fungi.

Claim 1 is indefinite and does not comply with Subsection 27(4) of the Patent Act. The repeated inclusion of the same element within a Markush group results in indefiniteness. "Substituted and unsubstituted alkyl" has been repeated during the defining of R_1 and R_2. This repetition must be removed.

Claim 1 is indefinite and does not comply with Subsection 27(4) of the Patent Act. The term "alkinyl" is unclear. The examiner believes that the applicant wishes to define alkynyl.

Claim 1 is indefinite and does not comply with Subsection 27(4) of the Patent Act. The expression "and their pharmaceutically acceptable salts, esters and salts of esters" is indefinite. The nature of the salts, ester and salts of the esters is unclear. The only acidic moiety defined with the claimed compounds is the phosphonic acid and its salts and esters have already been defined earlier in claim 1.

Claims 1 and 2 are indefinite and do not comply with Subsection 27(4) of the Patent Act. Possible substituents included in the term "substituted" are not defined in explicit and distinct terms, thus causing the scope of the claims to be indeterminable.

Claims 1 and 2 are broader in scope than the teaching of the description. To comply with Section 84 of the Patent Rules, the claim must specify that the alkyl and hydroxyalkyl groups being defined contain up to 9 carbon atoms (page 8, lines 22-30).

Claims 1-3 are indefinite and do not comply with Subsection 27(4) of the Patent Act. The functional groups "alkenyl", "alkinyl", "aryl", "acyl", "cycloalkyl", "aralkyl", "heterocyclic residue", "alkylene residue", "alkenylene residue", "hydroxyalkylene residue", "esters" and "alkanoyl" are not defined in explicit and distinct terms, thus causing the scope of the claims to be indeterminable. Definitions for "alkenyl", "alkynyl", "aryl", "acyl", "cycloalkyl", "aralkyl", "heterocyclic residue". "alkylene residue", "alkenyl residue" and "hydroxyalkylene residue" given in the description are inadequate since they do not define the functional groups in explicit terms, instead using the indefinite expressions "includes", "preferably", "may be" and "such as".

Claims 1, 3, 5, 6, 8 and 9 do not comply with Subsection 27(4) of the Patent Act. The inclusion of "in particular", "preferably", "particularly preferably" and "such as" causes a lack of clarity. Preferred embodiments should be defined in separate dependent claims.

Claim 2 is indefinite and does not comply with Subsection 27(4) of the Patent Act. "R_6" in formula (II) has not been defined.

Claims 2, 4 and 11 are indefinite and do not comply with Subsection 27(4) of the Patent Act. These claims contain a Markush group. In order to be Markush claims, they must end with the conjunction "and" before the last element of the list.

Claim 3 is indefinite and does not comply with Subsection 27(4) of the Patent Act. The definition of R_2 given in claim 1 does not support R_2 = acyl radical. Therefore, claim 3 does not comply with Section 87(3) of the Patent Rules as it does not include all the limitations contained in the claim to which it is dependent.

Claims 4 and 6 are indefinite and do not comply with Subsection 27(4) of the Patent Act. The structure of formula 2 in claim 2 does not contain an R_4 group. Therefore, claims 4 and 6 are improperly dependent on claim 2.

Claims 4, 5, 7 and 8 do not comply with Subsection 87(1) of the Patent Rules. Reference to preceding claims must be made by number.

Claim 7 is indefinite and does not comply with Subsection 27(4) of the Patent Act. "Wart" viruses is a layperson's term and should not be used to define the subject matter of the claims. In addition, the use of brackets causes ambiguity in terms of whether the applicant is attempting to claim papillomaviruses or all viruses that cause warts. The phrase "so called" is also indefinite and inappropriate.

Claim 7 is indefinite and does not comply with Subsection 27(4) of the Patent Act. The phrase "of the" on line 12 of claim 7 is unnecessary.

Claim 7 is indefinite and does not comply with Subsection 27(4) of the Patent Act. The repeated inclusion of same virus within a Markush group results in indefiniteness. The following have been repeated: hepatitis viruses, hepatitis B virus, hepatitis D viruses, hepatitis A virus, hepatitis E virus and hepatitis C virus. This repetition must be removed.

Claim 8 is indefinite and does not comply with Subsection 27(4) of the Patent Act. The use of the word "namely" causes the claim to become indefinite. It is unclear whether the applicant is attempting to define the subject matter of the claim broadly (unicellular parasites) or narrowly, limiting the subject matter to those unicellular parasites listed within the claim.

Claim 9 is indefinite and does not comply with Subsection 27(4) of the Patent Act. It is unclear how this claim further defines the subject matter of the preceding claims. Claims 1-8 define the

use of a compound to produce a pharmaceutical preparation. It is unclear how claim 9, which defines this use "in a pharmaceutical preparation" further defines the subject matter of claims 1-8.

Claim 9 is indefinite and does not comply with Subsection 27(4) of the Patent Act because of the term "effective content". When such a functional statement occurs in a claim, the medicinal utility of the composition of matter must be stated or be inherent from the preamble of the claim.

Claim 11 is indefinite and does not comply with Subsection 27(4) of the Patent Act. Cefazolin, cefuroxime, cefoxitin, cefotazime and cefalexine are all specific members of the cephalosporin family of antibiotics. As such, the meaning of "cefazolin group", "cefuroxime group", "cefoxitin group", "cefotazime group" and "cefalexine group" is unclear.

Claim 11 is indefinite and does not comply with Subsection 27(4) of the Patent Act. Claim 11 should specify that the one or more components are pharmaceutically active ingredients.

Claim 11 is indefinite and does not comply with Subsection 27(4) of the Patent Act. "Other cephalosporins", "new oral cephalosporins with expanded spectrum", "other B-lactam antibiotics" and "other diaminopyrimidine sulfonamide combinations" are indefinite. The words "new" and "other" are comparative terms for which there is no basis within claim 11.

Claim 11 is indefinite and does not comply with Subsection 27(4) of the Patent Act. The use of brackets around the term "quinolones" causes ambiguity in terms of whether the applicant is attempting to claim "quinolones" or all Gyrase inhibitors.

Claim 11 is indefinite and does not comply with Subsection 27(4) of the Patent Act. The dash in "quini-dines" is unnecessary.

Claim 11 is indefinite and does not comply with Subsection 27(4) of the Patent Act. "Arte mether", "arte ether" and "arte sunate" should all be one word.

Paragraph 80(1)(a) of the Patent Rules requires that the title be short and precise. "Use of aminoalkylphosphonic acid derivatives for the therapeutic and preventative treatment of infections" is a suitable title.

Under Subsection 81(3) of the Patent Rules, applicant must fully identify the documents referred to on page 20 and 25. A document so referred to should be identified at least by country, number and date for a published patent document, or by title, author, date, and source for non-patent documents. The document referred to as the "Red List" on page 20 and to Vial et al. on page 25 are not properly identified. In addition, the http internet address provided on page 20 defines a non-permanent electronic file and as such, does not constitute a permanently retrievable non-patent document. It is therefore an unacceptable source of documentation since access to the website is not guaranteed.

Under Paragraph 80(1)(e) of the Patent Rules, a brief statement of what each figure represents is needed.

In view of the foregoing defects, the applicant is requisitioned to amend the application in order to comply with the Patent Act and the Patent Rules or to provide arguments as to why the application does comply.

Under Section 34 of the Patent Rules, any amendment made in response to this requisition must be accompanied by a statement explaining the nature thereof, and how it overcomes each of the above objections.

Under Section 29 of the Patent Rules, applicant is requisitioned to provide an identification of any prior art cited in respect of the corresponding United States and European Patent Office applications and the patent numbers, if granted. Amendment to avoid references cited abroad may expedite the prosecution. If the particulars are not available to the applicant, the reason why must be stated. The above requisitioned information must be provided regardless of the current status of the foreign applications.

Under Section 29 of the Patent Rules, applicant is requisitioned to provide particulars of conflict, opposition, re-examination or similar proceedings in which the corresponding United States and European Patent Office applications may have been involved.

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